

OBJECTIVES: To evaluate, in daily practice, the benefits of drotrecogin alfa (DA) in the treatment of severe septic patients with multiple organ failure and optimum intensive care support. **METHODS:** In this prospective, observational pre-post study, the clinicians were free to include any patient meeting DA's inclusion criteria before and after DA's marketing. An optimal propensity score matching technique was used to reduce recruitment bias. Survival was modeled using a Cox proportional hazards model with a shared frailty term to account for the clustering of patients within the intensive care units. The number of bleeding events measured DA's safety. **RESULTS:** Respectively 509 and 587 patients were included in the before and after groups. There is strong evidence of recruitment bias: patients in the after group are younger, more frequently ventilated, have less comorbidities but more organ failures. After propensity score matching, 840 patients were retained in the analysis, with a better balance between the groups. The use of a frailty model improves significantly the variance explained by the survival model, showing a non-negligible cluster effect. When considering the whole sample of patients, without adjustments, survival is improved in the after (i.e. with DA) group ($p = 2.5\%$), with a hazard ratio (HR) of 0.805. In the matched sample, there are no significant survival differences (HR = 0.900, $p = 35.0\%$). However, after stratifying by the LODS severity score quartiles, significance is reached (HR = 0.795, $p = 4.8\%$). In the matched sample, a negative binomial model best described bleeding events. In this model, patients in the after group have a higher mean of bleeding events ($p = 2.0\%$). **CONCLUSION:** This observational study confirms DA's clinical trial results in the real practice setting. However, the use of the propensity score cannot replace randomization to assure perfect balance for all patient characteristics, measured and unmeasured. The results should therefore be considered with caution.

PIN2

ECONOMIC IMPLICATION OF HEPATITIS B VIRAL (HBV) LOAD REDUCTION FOR ENTECAVIR IN HEPATITIS B E ANTIGEN-POSITIVE CHRONIC HEPATITIS B (CHB) PATIENTS
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OBJECTIVES: To evaluate the cost effectiveness of entecavir in reducing HBV DNA viral load (VL) and subsequent compensated cirrhosis (CC), decompensate cirrhosis (DC), and hepatocellular cancer (HCC). **METHODS:** The analytic perspective was that of a third-party payer. We used patient-level drug exposure and VL data from a randomized phase III trial of 715 HBeAg+ CHB patients, and estimates of cost offsets and life expectancy gains as a result of the prevention of projected clinical events. The multivariate-adjusted relative risks with VL categories were estimated by Cox proportional hazards models from a Taiwan cohort of 3851 CHB subjects with 42,115 person-years of follow-up, and then applied to the trial patients whose VL were measured at Week 48 to estimate event risks. Entecavir and lamivudine were assigned daily prices of \$19.43 and \$6.14 respectively, based on recent First Data-Bank reports. Life expectancy for DC and HCC was estimated by the declining exponential approximation of life expectancy (DEALE) method. Other model parameter values were derived from external sources. The uncertainty surrounding event distribution and treatment failure rates beyond trial period were considered using probabilistic sensitivity analyses (PSA) with 1000 replicates. **RESULTS:** Subjects were male (75%), Asian (57%) or white (40%) with mean age 35 years. Entecavir was superior to

lamivudine for the proportion of subjects who achieved HBV DNA < 300 copies/ml by PCR assay at Week 48 (67% versus 37%, respectively) ($P < 0.05$). One year of entecavir therapy gained 0.7843 quality-adjusted life year (QALY) at an incremental cost of \$1607, with a 3% annual discount. Compared with lamivudine, using entecavir cost an incremental \$2049 per QALY gained (95%CI: \$688, \$5134), with 98.8% of PSA-derived estimates below \$10,000/QALY. Results are robust and most sensitive to treatment duration, efficacy, and cost. **CONCLUSIONS:** Entecavir given for one year is clinically effective and highly cost-effective in HBeAg+ patients.

PIN3

COST-EFFECTIVENESS ANALYSIS OF COMBINED THERAPY WITH PEGINTERFERON ALFA 2A (40KD) (PEGASYS®) AND RIBAVIRIN (COPEGUS®) IN PATIENTS WITH CHRONIC C HEPATITIS (CHC) AND PERSISTENTLY NORMAL ALT LEVELS (PNALT)

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OBJECTIVE: To establish the clinical prognosis, costs and cost-effectiveness of peginterferon alfa-2a (180mcg/week) plus ribavirin versus no treatment in patients with CHC and PNALT from a Spanish national health care system (NHS) perspective. **METHODS:** A Markov model was developed to simulate the disease progression of 45-year old patients with CHC and PNALT. Fibrosis progression rates in PNALT were obtained from published studies. Efficacy, in terms of sustained virological response (SVR), for peginterferon alfa-2a plus ribavirin and no treatment in patients with genotype 1 and genotype 2/3 was obtained from a multinational, randomized, controlled trial. In this trial, no patients in the control arm achieved an SVR. Transition probabilities and quality of life estimates were obtained from published literature. Unit costs were obtained from a Spanish database. The discount rate employed was 3.5%. **RESULTS:** In genotype 1 patients, peginterferon alfa-2a plus ribavirin compared with no treatment increases patients life expectancy by 0.63 years (0.70 quality-adjusted life years (QALYs)), yielding an incremental cost-effectiveness ratio (ICER) of 14,729 €/life year gained (LYG) (€13,388/QALY). In genotype 2/3 patients, peginterferon alfa-2a plus ribavirin increases life expectancy by 1.14 years (1.26 QALYs), yielding an ICER of 109 €/LYG (99 €/QALY). The overall ICER based on the genotype distribution in the trial is €11,374/LYG (€9952/QALY). **CONCLUSIONS:** From the Spanish NHS perspective, peginterferon alfa-2a (40KD) (PEGASYS®) plus ribavirin (COPEGUS®) in patients with CHC and PNALT is a cost-effective treatment option, regardless of HCV genotype.

PIN4

COST-EFFECTIVENESS ANALYSIS OF ALTERNATIVE ANTIMICROBIAL TREATMENTS FOR COMMUNITY-ACQUIRED PNEUMONIA (CAP)

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OBJECTIVE: To evaluate the cost-effectiveness of the empirical use of moxifloxacin in community-acquired pneumonia (CAP) taking into account clinical failure caused by prevailing levels of antimicrobial resistance in France, Germany and the US representing high, low and moderate levels of resistance respectively. **METHODS:** Only anecdotal evidence is available in the literature on the direct link between resistance and clinical failure. A

decision analytic model was developed to estimate clinical failure by studying the resistance mechanisms of three common CAP pathogens, *S.pneumoniae*, *H.influenzae* and the atypical pathogens. It was estimated that in most cases 95% of resistant pathogens would result in clinical failure. Country-specific resistance rates for moxifloxacin, macrolides, beta-lactams and doxycycline were obtained from surveillance studies. Multi-drug resistance was estimated using US multi-drug resistance rates. Treatment algorithms were partially based on CAP treatment guidelines for out-patients of the Fine risk categories, I to III, focusing on mono-therapy. Patients could receive up to two treatments in the community and one hospitalisation. The outcomes evaluated were clinical failure avoided, hospitalisations avoided and second-line treatments avoided. Resource use and costs were obtained from the literature. Expert opinion was used extensively to validate the clinical assumptions. **RESULTS:** Moxifloxacin dominated all other treatments in France and the US and roxithromycin and cefuroxim strategies in Germany. Clinical failure rates for moxifloxacin and macrolide strategies were 5.3% and 47.3% in France, 5.2% and 16.8% in Germany and 5.2% and 23.6% the US respectively. In Germany compared to a strategy of amoxicillin followed by roxithromycin, moxifloxacin had an incremental cost-effectiveness of €1 per clinical failure avoided, but prevented 9646 clinical failures and 918 hospitalisations per 100,000 patients. **CONCLUSIONS:** Antimicrobial resistance has a significant impact on the cost-effectiveness of empirical treatment of CAP. The first-line use of moxifloxacin in CAP is a cost-effective strategy for all levels of resistance.

PINS

DYNAMIC MODELLING FOR ESTIMATING THE COST-EFFECTIVENESS OF A CHLAMYDIA TRACHOMATIS SCREENING PROGRAM

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OBJECTIVES: To estimate the cost-effectiveness of a systematic Chlamydia trachomatis (CT) screening program including partner treatment for The Netherlands using a dynamic approach. **METHODS:** Data on infection prevalence, participation rates and sexual behaviour were obtained from a large pilot study conducted in The Netherlands. We developed a dynamic SIS (Susceptible-Infected-Susceptible) model, which is widely used in exploring the transmission dynamics of infectious diseases, to estimate the impact of screening men and women on the incidence and prevalence of CT in the population. Subsequently, a progression-of-disease tree was used to calculate the complications averted by the screening program. Cost-effectiveness is expressed as the net costs per major outcome averted (MOA). We compared doing nothing both with a one-off screening program and with screening on various time intervals. **RESULTS:** Compared to do-nothing the one-off screening program is estimated to cost €373 per MOA. However, restricting the screening to women only the program is estimated to save costs. Even though screening on various time intervals adverts more serious complications, this is less cost effective as the screening related costs increase relatively more (e.g. bi-annual screening is estimated to cost €3200 per MOA compared to do-nothing). **CONCLUSION:** Our cost-effectiveness analysis shows that society has net to pay for the prevention of CT complications. A one-off screening program is however more cost-effective than screening on various time intervals. One could argue that €373 per MOA, for the one-off screening program, is

an acceptable cost-effectiveness. A screening program consisting of screening women only should always be adopted from a pharmacoeconomic point of view.

PIN6

INFECTIONS CAUSED BY RESISTANT CANDIDA SPECIES: COST-MINIMIZATION ANALYSIS OF ANTIFUNGAL THERAPY IN BRAZIL

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OBJECTIVE: Compare the total costs of antifungal therapy—lipid formulation of Amphotericin B (LAB), voriconazole (VCZ) and caspofungin (CAS)—as empirical treatment in Brazilian institutions/patients with high risk of infection by fluconazole-resistant *Candida* species. **METHODS:** A Brazilian analytical model was constructed using the recommended protocols for resistant *Candida* infections in a 60-kg hypothetical patient and 21 days of treatment. The analysis perspective was from the third-party payers. Drug and device prices were retail prices (database: April/2005) including taxes. The daily imputations values used (without diagnostic tests and procedures) were obtained from hospital consultants (average of costs from medium-level hospitals in Sao Paulo). The studied scenarios were: 1) continuous use of intravenous therapy in full-time inpatient condition; 2) switch from IV to oral with voriconazole in full-time inpatient condition; and 3) switch from IV to oral with voriconazole and early discharge. **RESULTS:** The cumulative cost for LAB was R\$81,080.37/US\$32,432.15 and for CAS was R\$ 50,697.38/US\$20,278.95, without changes in all scenarios. Cumulative cost of VCZ has changed in each scenario and was R\$38,382.34/US\$15,352.94, R\$26,991.93/US\$10,796.77 and R\$23,856.44/US\$9542.58 for the scenarios 1, 2, and 3, respectively. **CONCLUSION:** In high risk *Candida*-resistant scenario, VCZ has the lower cumulative cost than CAS and LAB (scenario 1). If the clinical situation allows the use of oral formulation, the advantage of VCZ increases significantly (scenario 2), mainly if the clinical status of patients permits discharge (scenario 3). Moreover, the oral and/or home treatment could reduce the risk of nosocomial infection, morbidity/mortality for immunocompromised patients and improve the QoL, but we couldn't measure these impacts because of lack of epidemiologic data in Brazil.

PIN7

